רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

Venclexta 10 mg tablets; Venclexta 50 mg tablets; Venclexta 100 mg tablets

ונקלקסטה 10 מ"ג טבליות ; ונקלקסטה 50 מ"ג טבליות ;ונקלקסטה 100 מ"ג טבליות

Film coated tablets

venetoclax 10 mg; venetoclax 50 mg; venetoclax 100 mg

חברת .AbbVie Biopharmaceuticals Ltd מבקשת להודיע כי העלונים לרופא ולצרכן של התכשירים עודכנו. בהודעה זו מצוינים סעיפים בהם נעשה שינוי מהותי או שינוי המהווה החמרה (שינוי שהינו הוספה מסומן בקו תחתון, מחיקה מסומנת בקו אמצעי). עדכונים נוספים אשר אינם מהווים החמרה או שאינם מהותיים, אינם נכללים בהודעה זו.

ההתוויה המאושרת לתכשיר:

Venclexta is indicated for the treatment of:

- patients with chronic lymphocytic leukemia (CLL) with 17p deletion, who have received at least one prior therapy.
- patients with relapsed or refractory CLLwho have failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor.

<u>העלון לצרכן עודכן בסעיפים הבאים:</u>

- **ונקלקסטה ותרופות אחרות**

.....
ספר לרופא או לרוקח שלך אם אתה לוקח אחת מהתרופות הבאות משום שהן יכולות להעלות או להפחית את הכמות של ונקלקסטה בדמך:

- אנטיביוטיקה לטיפול בזיהומים חיידקיים - קלאריתרומיצין, ציפרופלוקסצין, אריתרומיצין, נאפצילין, ~~אזיתרומיצין~~ או ריפאמפיצין
.....

<u>העלון לרופא עודכן בסעיפים הבאים:</u>

- **5.5 Effects on ability to drive and use machines**

<u>VENCLEXTA has no or negligible influence on the ability to drive and use machines. Fatigue has been reported in some patients taking VENCLEXTA and should be considered when assessing a patient's ability to drive or operate machines.</u>

- **7.1 Effects of Other Drugs on VENCLEXTA**

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Strong CYP3A Inhibitors

Concomitant use of VENCLEXTA with strong CYP3A inhibitors (e.g., ketoconazole, conivaptan, clarithromycin, indinavir, itraconazole, lopinavir, ritonavir, telaprevir, posaconazole and voriconazole) at initiation and during ramp-up phase is contraindicated *[see Contraindications (4) and Clinical Pharmacology (12.3)]*

For patients who have completed the ramp-up phase and are on a steady daily dose of VENCLEXTA, reduce the VENCLEXTA dose by at least 75% when used concomitantly with strong CYP3A inhibitors. Resume the VENCLEXTA dose that was used prior to initiating the CYP3A inhibitor 2 to 3 days after discontinuation of the inhibitor *[see Dosage and Administration (2.3, 2.4) and Clinical Pharmacology (12.3)]*.

<u>Co-administration of ritonavir increased venetoclax Cmax by 2.4-fold and AUC by 7.9-fold.</u>

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Moderate CYP3A Inhibitors and P-gp Inhibitors

Avoid concomitant use of moderate CYP3A inhibitors (e.g., erythromycin, ciprofloxacin, diltiazem, dronedarone, fluconazole, verapamil) or P-gp inhibitors (e.g., amiodarone, ~~azithromycin,~~ captopril, carvedilol, cyclosporine, felodipine, quercetin, quinidine, ranolazine, ticagrelor) with VENCLEXTA. Consider alternative treatments. If a moderate CYP3A inhibitor or a P-gp inhibitor must be used, reduce the VENCLEXTA dose by at least 50%. Monitor patients more closely for signs of VENCLEXTA toxicities [see Dosage and Administration (2.3, 2.4) and Clinical Pharmacology (12.3)].

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- **7.2 Effects of VENCLEXTA on Other Drugs**

P-gp substrates

Administration of a single 100 mg dose of venetoclax with digoxin resulted in a 35% increase in digoxin Cmax and a 9% increase in AUC∞. ~~In vitro data suggest venetoclax has inhibition potential on P-gp substrates at therapeutic dose levels in the gut.~~ Therefore, co-administration of narrow therapeutic index P-gp substrates (e.g., digoxin, everolimus, and sirolimus) with VENCLEXTA should be avoided. If a narrow therapeutic index P-gp substrate must be used, it should be taken at least 6 hours before VENCLEXTA.

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- **12.3 Pharmacokinetics**

Drug Interactions

Ritonavir

Co-administration of 50 mg once daily ritonavir, a strong CYP3A, P-gp and OATP1B1/B3 inhibitor, for 14 days in 6 healthy subjects increased venetoclax Cmax by 2.4-fold and AUC by 7.9-fold [see Drug Interactions (7.1)].

Azithromycin

In a drug-drug interaction study in 12 healthy subjects, co-administration of 500 mg of azithromycin on the first day followed by 250 mg of azithromycin for 4 days decreased venetoclax Cmax by 25% and AUC∞ by 35%. No dose adjustment is needed when venetoclax is co-administered with azithromycin

Digoxin

In a drug-drug interaction study in 10 healthy subjects, administration of a single 100 mg dose of venetoclax with 0.5 mg digoxin, a P-gp substrate, resulted in a 35% increase in digoxin Cmax and a 9% increase in AUC∞ [see Drug Interactions (7.2)].

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In vitro Studies

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Venetoclax is a P-gp and BCRP substrate as well as a P-gp and BCRP inhibitor and weak OATP1B1 inhibitor in vitro. ~~To avoid a potential interaction in the gastrointestinal tract, co-administration of narrow therapeutic index P-gp substrates such as digoxin with VENCLEXTA should be avoided. If a narrow therapeutic index P-gp substrate must be used, it should be taken at least 6 hours before VENCLEXTA.~~ Venetoclax is not expected to inhibit OATP1B3, OCT1, OCT2, OAT1, OAT3, MATE1, or MATE2K at clinically relevant concentrations.

העלונים המעודכנים לרופא ולצרכן נשלחו למאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, AbbVie Biopharmaceuticals Ltd, רחוב החרש 4, הוד השרון או בטלפון 09 – 7909600.

בברכה,
חופית שוורץ - רוקחת ממונה